

REMARKS

Favorable reconsideration and allowance of this application are requested.

1. Claim Status

The claims pending in this application are claims 1-21 which were submitted by the USPTO's electronic filing system as part of the applicants' Second Preliminary Amendment dated April 8, 2008, and which apparently were not considered by the Examiner prior to issuance of his April 14, 2008 Office Action.¹ Therefore, any further written action that may be deemed necessary must be non-final since not all pending claims have been acted upon at this juncture. However, as will be evident from the following discussion, no such further action will in fact be needed as the claims now pending herein are patentably distinguishable over the applied art of record.

2. Response to 35 USC §102(b) Rejection

The only issue to be resolved in this application is the Examiner's rejection of claims 1-15 under 35 USC §102(b) as allegedly anticipated by Kimel et al (USP 3,250,778). Applicants emphatically disagree with this conclusion and submit that all claims pending in this application are patentable over Kimel et al.

The present application claims a process for the preparation of pyrido[3,4][1,3]dioxepins of formula I (and optionally a process for manufacturing pyridxine) by:

¹ That the Second Preliminary Amendment is in fact present in the file history of the subject application can be ascertained from the USPTO PAIR system at https://spportal.uspto.gov/secure/myportal/l/u/p/kcxml/04_Sj9SPyksy0xPLMrMz0vM0Y_QjzKLN4gPNgXJgFg_-ofgRqCLGpugijnABX4_83FT9IKBEpDIQxNHDHV8gJzU9MbISP1jfWz9AvyA3NDSi3NsRAGmFd0Q!/delta/_base64xml/L0JSk03dWIDU1IKSi9vQXd3QUFNWwdB00VJUWhDRUVJaEzLQSEvNEZH2RZbkIKMEZSb1hmckNIZGgvN18wXzFMNS8xMS9zYS5nZXRCaWI#7_0_1L5

- (a) mixing an oxazole of formula II with a dioxepin of formula III in the substantial absence of a solvent and a catalyst to give a mixture of two adducts IV (major proportion) and V (minor proportion),
- (b) removing unreacted starting materials II and III by distillation under reduced pressure,
- (c) adding a substantially anhydrous organic acid to the mixture,
- (d) removal of the generated alkanol R¹OH by distillation under reduced pressure, and
- (e) acylation with a carboxylic acid anhydride.

Kimmel et al fails to disclose or suggest steps (b), (c) and/or (e) which is practiced by the present invention and thus for this reason alone cannot anticipate the presently claimed invention.

Moreover, it will be observed that Example 21 of Kimmel et al describes in detail the preparation of crude pyridoxol hydrochloride (no yield given) by heating 4-methyl-6-ethoxy-oxazole (a compound of formula II wherein R1 is ethyl) with 4,7-dihydro-2-isopropyl-3-dioxepin (a compound of formula III wherein R2 is hydrogen and R3 is isopropyl). After cooling the reaction mixture was rinsed out of the reaction vessel with methanol. The solution was concentrated in vacuo. 2N aqueous HCl was added and the solution obtained was again concentrated in vacuo. The residue was dissolved in ethanol and to the solution were added ethanolic HCl and water. From this solution pyridoxol hydrochloride crystallized and was obtained as crude product.

The Example therefore does not disclose or even remotely suggest employing steps (b), (c), and (e) as claimed by the present applicants. Perhaps most telling of the total lack of disclosure in Kimmel et al is the absence of step (c), that is the use of a

substantially **anhydrous** acid. Nowhere in Kimmel et al is there even remotely suggested that an **anhydrous** acid may be employed in the reaction scheme.

Moreover, Kimmel et al actually teach away from the use of *any* acid. Specifically, as noted in column 2, line 68 bridging column 3, line 8, Kimmel et al actually teach away from use of *an* acid catalyst. That is, while Kimmel et al acknowledge that the reaction may be acid catalyzed with acetic acid, trichloroacetic acid, p-toluenesulfonic acid or the like (col. 2, lines 68-69), Kimmel et al go on to state that:

"The use of [acids such as acetic acid trichloroacetic acid, p-toluenesulfonic acid or the like] is, however, *not* preferred since the oxazole starting materials of Formula IV are acid sensitive at the reaction temperatures utilized. (Col. 2, line 71 through col. 3, line 1, emphasis added.)

Thus, Kimmel et al go on to observe that the therein disclosed reaction scheme is "...advantageously self-catalyzed, i.e., the end product of Formula II serves to catalyze the reaction of a compound of Formula III with a compound of Formula IV to produce the end product of Formula II." (Col. 3, lines 2-6)

Therefore, not only does Kimmel et al *not* anticipate the presently pending claims, Kimmel et al actually teaches away from a significant distinguishing aspect of the same – that is, the use of **anhydrous** acid.

Withdrawal of the rejection advanced on the basis of Kimmel et al is therefore in order.

FISCHESSER et al
Serial No. 10/579,836
July 10, 2008

6. Fee Authorization

The Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, in the fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Account No. 14-1140.

Respectfully submitted,

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